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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/310,667	Applicant(s) ECKER ET AL.	
	Examiner Frank Lu	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-29,35-41 and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-29,35-41 and 43-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 January 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

DETAILED ACTION

CONTINUED EXAMINATION UNDER 37 CFR 1.114 AFTER FINAL REJECTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 20, 2002 has been entered. The claims pending in this application are claims 27-29, 35-41, and 43-67. Rejection and/ or objection not reiterated from the previous office action are hereby withdrawn. The following rejections are based on amendment.

Oath/Declaration

2. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the inventor, Ranga Sampath, changed his/her address and citizenship without an initial. See 37 CFR 1.52(c)

Specification

3. The substitute specification filed on March 20, 2002 has not been entered and a substitute specification excluding the claims is required pursuant to 37 CFR 1.125(a) because the number or nature of the amendments (see pages 42-70 of applicant's amendment filed on March 20, 2002, too much changes) renders it difficult to consider the application, or to arrange the papers for printing or copying (See MPEP § 608.01(q)).

A substitute specification filed under 37 CFR 1.125(a) must only contain subject matter from the original specification and any previously entered amendment under 37 CFR 1.121. If the substitute specification contains additional subject matter not of record, the substitute specification must be filed under 37 CFR 1.125(b) and must be accompanied by: 1) a statement that the substitute specification contains no new matter; and 2) a marked-up copy showing the amendments to be made via the substitute specification relative to the specification at the time the substitute specification is filed.

Drawings

4. The formal drawings submitted on January 16, 2002 have been disapproved because they introduce new matter into the drawings. 37 CFR 1.121(a)(6) states that no amendment may introduce new matter into the disclosure of an application. The added or deleted materials in Figures 3, 4, 5A and 5B which are not supported by the original disclosure is as follows:
(1) in newly submitted Figure 3 , "Parse Blast Results" was no longer directly connected with "Accession Numbers from Blast results".

(2) in newly submitted Figure 4, "Bin all results according to user-defined choices from annotations and e-values" was replaced with "Bin according to user-preferences".

(3) in newly submitted Figure 5A ,"Go to Fig. 5B" was replaced with " Go to Page 2 " and "No" between "Generate Compare Array for windowSize =currWindow " and "currWin>=maxWin" was deleted.

(4) in newly submitted Figure 5B, " End of Alignment" was directly connected with "No".

(5) in newly submitted Figure 5B, "Add Hit to Report" was directly connected with " For each Position on Alignment".

(6) in newly submitted Figure 5B, "Set lastWasHit =true, Record Start of HitRegion" was directly connected with " For each Position on Alignment".

Applicant is required to cancel these new matters in the reply to this Office Action.

Claim Rejections - 35 U.S.C. § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes iron response element and 3' untranslated region of the histone mRNA (see specification, pages 32-38), the specification does not adequately describe that : (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; and (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Response to Arguments

In page 35, third paragraph bridging to page 36, first paragraph of applicant's remarks, applicant argued that one having ordinary skill in the art would have known that, in view of the description of 3' untranslated region of the histone mRNA in the prior art and the specification, "applicant's claimed invention did not include the 3' untranslated region of the histone mRNA".

This arguments has been fully considered but it is not persuasive toward the withdrawal of the rejection. First, although the specification describes 3' untranslated region of the histone mRNA (see specification, pages 37 and 38), the specification does not adequately describe that : (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; and (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67. In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. On other word, one skilled in the art will not recognize "applicant's claimed invention did not include the 3' untranslated region of the histone mRNA". Second, applicant did not indicate, in the specification, where described an oligonucleotide comprising a molecular interaction site that was present in the RNA did not comprise the iron response element and an oligonucleotide comprising a molecular interaction site that was present in the RNA did not comprise the iron response element or the 3' untranslated region of the histone mRNA.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 50 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 50 and 66 recite the limitation "said other nucleic acids" in the claims. There is insufficient antecedent basis for this limitation in the claims since claims 38 and 55 do not have "other nucleic acids" ("further nucleic acids " in claims 50 and 66 is considered to be different from "other nucleic acids").

Claim Rejections - 35 U.S.C. § 102/103

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 35-40, 43-57, and 59-67 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Manzella *et al.*, (J. Biol. Chem., 267, 7077-7082, 1992).

Manzella *et al.*, teach binding of a specific protein(s) to a conserved region of the ornithine decarboxylase mRNA 5'-untranslated region. In this study, one or more cellular protein(s) (ornithine decarboxylase mRNA 5'-UTR binding protein (ODCBP)), that bound specifically to a conserved region of the 5'- untranslated region (5'-UTR) of rat ornithine decarboxylase (ODC) mRNA as recited in claims 35, 40, 51, 52, 57, and 67 was identified using a RNA gel retardation assay. A similar binding activities was found in cytoplasmic extracts from a variety of animal cells and tissues such as human tumor cells, mouse and rat fibroblast, and cow brain as recited in claims 35, 39, 51, 52, 56, and 67 (see pages 7077-7080). Note that: (1) although Manzella *et al.*, did not directly disclose that modulation of the expression of ornithine decarboxylase mRNA by binding of a protein cytoplasmic extracts to ornithine decarboxylase mRNA 5'-UTR as recited in claims 35, 51, 52, and 67, in the absence of convincing evidence to

the contrary, this limitation was considered to be an inherent property of ornithine decarboxylase mRNA since there was no structural difference between ornithine decarboxylase mRNA and claimed oligonucleotde recited in claims 35, 51, 52, and 67; and (2) although the molecular interaction site taught by Manzella *et al.*,was not identified by the method recited in claims 35-38, 43-55, and 59-67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

13. Claims 27-29, 35-38, 41, 43-55, and 58-67 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Garcia *et al.*, (J. Mol. Biol. 254, 247-259, 1995) in light of Molecule Cell Biology (second Edition, edited by Darnell et al., pages 99-101, 1990) and Textbook of Biochemistry with clinical correlations (third edition, Edited by Thomas Devlin, 1992, page 739).

Garcia *et al.*, teach solution structure of the ribosome-binding domain of *E. coli* translation initiation factor IF3. As acknowledged by Garcia, in prokaryotic organisms, the first step in the initiation of protein translation was the binding of the 3' region of the 16S ribosomal RNA to the complementary 'Shine & Dalgarno' sequence located a few bases upstream to the start codon of mRNA. This ensured a pre-positioning of the 30S ribosome (see page 247).

Note that: (1) although Garcia *et al.,* did not directly show to this interaction was specific for prokaryotic organisms as described claims 27, 41, and 58, this limitation was considered as inherent to the reference taught by Garcia *et al.*, since it was known that eukaryotes did not utilize this mRNA-rRNA base pair mechanism and 'Shine & Dalgarno' sequence was only found in prokaryotic organisms, not in eukaryotic RNA and human RNA as recited in claims 28 and 29 and the interaction between IF3 and 30S subunit of the ribosome was specific for prokaryotic organisms (see right column in page 248; Molecule Cell Biology, second Edition, edited by Darnell et al., pages 99-101; Textbook of Biochemistry with clinical correlations, third edition, Edited by Thomas Devlin, page 739); (2) "Shine & Dalgarno" sequence in mRNA that could bind to 16S RNA to could be considered as a molecular interaction site as recited in claims 35, 51, 52, and 67; (3) the binding of the 3' region of the 16S ribosomal RNA to the complementary 'Shine & Dalgarno' sequence located a few bases upstream to the start codon of mRNA could be considered to modulate mRNA expression as recited in claims 27, 35, 51, 52, and 67; and (4) although the molecular interaction site taught by Garcia *et al., et al.,*was not identified by the methods recited in claims 35-38, 43-55, and 59-67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process."*In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Response to Arguments

In page 38, second paragraph bridging to page 39, second paragraph of applicant's remarks, applicant argued that: (1) "the Garcia reference fails to teach or suggest an oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site, as recited in claims 27 and 35 " since " the 16S RNA molecule that is relied on for the instant rejection is not an oligonucleotide, as called for by the claims."; (2) "[T]he Garcia reference further fails to teach or suggest that the molecular interaction site of the 16S RNA is present in 'least one additional prokaryotic RNA,' as recited in the claims." ; and (3) "the Office Action fails to provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of claimed invention.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, Garcia *et al.,* did teach an oligonucleotide that comprises a molecular interaction site since a nucleotide sequence comprising Shine & Dalgarno sequence in mRNA or a nucleotide sequence comprising its complementary sequence in 16 S RNA could be considered as an oligonucleotide comprising a molecular interaction site that was present in the RNA of a selected organism as recited in claims 27 and 35. Second, although Garcia reference did not directly show that the molecular interaction site of the 16S RNA or mRNA was present in "least one additional prokaryotic RNA", it was known that all bacteria mRNA had Shine & Dalgarno sequence and small RNA as 16S RNA in bacteria had complementary sequence of Shine & Dalgarno sequence (see Molecule Cell Biology, second Edition, edited by Darnell et al.,

page 99, 1990). Third, the Office Action did not need to "provide a reason as to why one of ordinary skill in the art would have been led to modify the ribosomal subunit of the Garcia reference to arrive at the oligonucleotide of claimed invention." since Garcia *et al.,* in light of the textbook of Molecule Cell Biology and Textbook of Biochemistry with clinical correlations taught claimed invention.

Conclusion

14. No claim is allowed.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
June 6, 2002